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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 09	CA/CAPlus records now contain indexing from 1907 to the present
NEWS	4	DEC 08	INPADOC: Legal Status data reloaded
NEWS	5	SEP 29	DISSABS now available on STN
NEWS	6	OCT 10	PCTFULL: Two new display fields added
NEWS	7	OCT 21	BIOSIS file reloaded and enhanced
NEWS	8	OCT 28	BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS	9	NOV 24	MSDS-CCOHS file reloaded
NEWS	10	DEC 08	CABA reloaded with left truncation
NEWS	11	DEC 08	IMS file names changed
NEWS	12	DEC 09	Experimental property data collected by CAS now available in REGISTRY
NEWS	13	DEC 09	STN Entry Date available for display in REGISTRY and CA/CAPlus
NEWS	14	DEC 17	DGENE: Two new display fields added
NEWS	15	DEC 18	BIOTECHNO no longer updated
NEWS	16	DEC 19	CROPU no longer updated; subscriber discount no longer available
NEWS	17	DEC 22	Additional INPI reactions and pre-1907 documents added to CAS databases
NEWS	18	DEC 22	IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
NEWS	19	DEC 22	ABI-INFORM now available on STN
NEWS	20	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS	21	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAPlus
NEWS	22	FEB 05	German (DE) application and patent publication number format changes
NEWS	23	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS	24	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	25	MAR 03	FRANCEPAT now available on STN
NEWS EXPRESS			MARCH 5 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 3 MARCH 2004
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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 14:53:21 ON 11 MAR 2004

=> FIL MEDLINE BIOSIS EMBASE CA SCISEARCH
COST IN U.S. DOLLARS

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FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 14:53:35 ON 11 MAR 2004

FILE 'BIOSIS' ENTERED AT 14:53:35 ON 11 MAR 2004
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FILE 'SCISEARCH' ENTERED AT 14:53:35 ON 11 MAR 2004
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=> s polyamin? or putrescin? or (diamino? (n) (propan? or butan? or heptan? or octan?))

L1 109204 POLYAMIN? OR PUTRESCIN? OR (DIAMINO? (N) (PROPAN? OR BUTAN? OR HEPTAN? OR OCTAN?))

=> s apoptosi? (s) (prevent? or reduc? or inhib? or attenu?)
3 FILES SEARCHED...

L2 148129 APOPTOSI? (S) (PREVENT? OR REDUC? OR INHIB? OR ATTENU?)

=> s l1 (s) l2

L3 491 L1 (S) L2

=> s l1 (5n) l2

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L1 (5A) L7'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L2 (5A) L8'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L3 (5A) L9'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L4 (5A) L10'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L5 (5A) L11'
L4 629 L1 (5N) L2

=> s apoptosi? (5n) (prevent? or reduc? or inhib? or attenu?)
3 FILES SEARCHED...

L5 84362 APOPTOSI? (5N) (PREVENT? OR REDUC? OR INHIB? OR ATTENU?)

=> s l1 (5n) l2

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L1 (5A) L7'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L2 (5A) L8'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L3 (5A) L9'

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L4 (5A) L10'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L5 (5A) L11'
L6 629 L1 (5N) L2

=> s l1 (5n) l5
L7 159 L1 (5N) L5

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8 55 DUP REM L7 (104 DUPLICATES REMOVED)

=> s l8 and Py=<2001
2 FILES SEARCHED...
L9 41 L8 AND PY=<2001

=> d his

(FILE 'HOME' ENTERED AT 14:53:21 ON 11 MAR 2004)

FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 14:53:35 ON 11
MAR 2004

L1 109204 S POLYAMIN? OR PUTRESCIN? OR (DIAMINO? (N) (PROPAN? OR BUTAN? O
L2 148129 S APOPTOSI? (S) (PREVENT? OR REDUC? OR INHIB? OR ATTENU?)
L3 491 S L1 (S) L2
L4 629 S L1 (5N) L2
L5 84362 S APOPTOSI? (5N) (PREVENT? OR REDUC? OR INHIB? OR ATTENU?)
L6 629 S L1 (5N) L2
L7 159 S L1 (5N) L5
L8 55 DUP REM L7 (104 DUPLICATES REMOVED)
L9 41 S L8 AND PY=<2001

=> s l7 and eIF5a?
L10 0 L7 AND EIF5A?

=> s l1 and (eif5a or eIF (n) 5a)
L11 188 L1 AND (EIF5A OR EIF (N) 5A)

=> s l11 and l5
L12 2 L11 AND L5

=> d l12 1-2 ibib abs

L12 ANSWER 1 OF 2 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 1998001039 EMBASE

TITLE: Excess **putrescine** accumulation inhibits the
formation of modified eukaryotic initiation factor
5A (eIF-5A) and induces
apoptosis.

AUTHOR: Tome M.E.; Fiser S.M.; Payne C.M.; Gerner E.W.

CORPORATE SOURCE: E.W. Gerner, Department of Radiation Oncology, Arizona
Health Sciences Center, University of Arizona, Tucson, AZ
85724

SOURCE: Biochemical Journal, (1997) 328/3 (847-854).
Refs: 62

ISSN: 0264-6021 CODEN: BIJOAK

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB DH23A cells, an α -difluoromethylornithine-resistant variant of the

parental hepatoma tissue culture cells, express high levels of stable ornithine decarboxylase. Aberrantly high expression of ornithine decarboxylase results in a large accumulation of endogenous **putrescine** and increased apoptosis in DH23A cells when α -difluoromethylornithine is removed from the culture. Treatment of DH23A cells with exogenous **putrescine** in the presence of α -difluoromethylornithine mimics the effect of drug removal, suggesting that **putrescine** is a causative agent or trigger of **apoptosis**. Accumulation of excess intracellular **putrescine** **inhibits** the formation of hypusine in vivo, a reaction that proceeds by the transfer of the butylamine moiety of spermidine to a lysine residue in eukaryotic initiation factor **5A (eIF-5A)**. Treatment of DH23A cells with diaminoheptane, a competitive inhibitor of the post-translational modification of **eIF-5A**, causes both the suppression of **eIF-5A** modification in vivo and induction of apoptosis. These data support the hypothesis that rapid degradation of ornithine decarboxylase is a protective mechanism to avoid cell toxicity from **putrescine** accumulation. Further, these data suggest that suppression of modified **eIF-5A** formation is one mechanism by which cells may be induced to undergo apoptosis.

L12 ANSWER 2 OF 2 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 1998:46733 SCISEARCH

THE GENUINE ARTICLE: YN845

TITLE: Excess **putrescine** accumulation inhibits the formation of modified eukaryotic initiation factor **5A (eIF-5A)** and induces apoptosis

AUTHOR: Tome M E; Fiser S M; Payne C M; Gerner E W (Reprint)
CORPORATE SOURCE: UNIV ARIZONA, ARIZONA HLTH SCI CTR, DEPT RADIAT ONCOL, TUCSON, AZ 85724 (Reprint); UNIV ARIZONA, ARIZONA HLTH SCI CTR, DEPT RADIAT ONCOL, TUCSON, AZ 85724; UNIV ARIZONA, ARIZONA HLTH SCI CTR, DEPT BIOCHEM, TUCSON, AZ 85724; UNIV ARIZONA, ARIZONA RES LABS, TUCSON, AZ 85724

COUNTRY OF AUTHOR: USA

SOURCE: BIOCHEMICAL JOURNAL, (15 DEC 1997) Vol. 328, Part 3, pp. 847-854.
Publisher: PORTLAND PRESS, 59 PORTLAND PLACE, LONDON, ENGLAND W1N 3AJ.
ISSN: 0264-6021.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 63

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB DH23A cells, an alpha-difluoromethylornithine-resistant variant of the parental hepatoma tissue culture cells, express high levels of stable ornithine decarboxylase. Aberrantly high expression of ornithine decarboxylase results in a large accumulation of endogenous **putrescine** and increased apoptosis in DH23A cells when alpha-difluoromethylornithine is removed from the culture. Treatment of DH23A cells with exogenous **putrescine** in the presence of alpha-difluoromethylornithine mimics the effect of drug removal, suggesting that **putrescine** is a causative agent or trigger of **apoptosis**. Accumulation of excess intracellular **putrescine** **inhibits** the formation of hypusine in vivo, a reaction that proceeds by the transfer of the butylamine moiety of spermidine to a lysine residue in eukaryotic initiation factor **5A (eIF-5A)**. Treatment of DH23A cells with diaminoheptane, a competitive inhibitor of the post-translational modification of **eIF-5A**, causes both the suppression of **eIF-5A** modification in vivo and induction of apoptosis. These data support the hypothesis that rapid degradation of ornithine decarboxylase

is a protective mechanism to avoid cell toxicity from **putrescine** accumulation. Further, these data suggest that suppression of modified **EIF-5A** formation is one mechanism by which cells may be induced to undergo apoptosis.

=> d his

(FILE 'HOME' ENTERED AT 14:53:21 ON 11 MAR 2004)

FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 14:53:35 ON 11 MAR 2004

L1 109204 S POLYAMIN? OR PUTRESCIN? OR (DIAMINO? (N) (PROPAN? OR BUTAN? O
L2 148129 S APOPTOSI? (S) (PREVENT? OR REDUC? OR INHIB? OR ATTENU?)
L3 491 S L1 (S) L2
L4 629 S L1 (5N) L2
L5 84362 S APOPTOSI? (5N) (PREVENT? OR REDUC? OR INHIB? OR ATTENU?)
L6 629 S L1 (5N) L2
L7 159 S L1 (5N) L5
L8 55 DUP REM L7 (104 DUPLICATES REMOVED)
L9 41 S L8 AND PY=<2001
L10 0 S L7 AND EIF5A?
L11 188 S L1 AND (EIF5A OR EIF (N) 5A)
L12 2 S L11 AND L5

=> d l9 ibib abs 1-41

L9 ANSWER 1 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2001685069 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11590175
TITLE: Polyamine depletion induces rapid NF-kappa B activation in IEC-6 cells.
AUTHOR: Pfeiffer L M; Yang C H; Murti A; McCormack S A; Viar M J; Ray R M; Johnson L R
CORPORATE SOURCE: Department of Pathology, University of Tennessee Health Science Center, Memphis, Tennessee 38163, USA.. lpfeffer@utmem.edu
CONTRACT NUMBER: CA73753 (NCI)
DK-16505 (NIDDK)
SOURCE: Journal of biological chemistry, (2001 Dec 7) 276 (49) 45909-13.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011204
Last Updated on STN: 20020919
Entered Medline: 20020110

AB The proliferation of the rat intestinal mucosal IEC-6 cell line requires polyamines, whose synthesis is catalyzed by the enzyme ornithine decarboxylase (ODC). ODC inhibition leads to **polyamine** depletion, as well as **inhibition** of both cell proliferation and **apoptosis** by regulating gene expression. The NF-kappa B transcription factor regulates genes involved in apoptotic, immune, and inflammatory responses. In the present study we tested the hypothesis that NF-kappa B is activated following ODC inhibition. We found that the inhibition of ODC by alpha-difluoromethylornithine (DFMO) resulted in a approximately 50% decrease in intracellular putrescine levels within 1 h. NF-kappa B is activated by DFMO through the degradation of the inhibitory protein I kappa B alpha that sequesters NF-kappa B in the cytoplasm. The DFMO-induced NF-kappa B complexes contain the p65 and p50 members of the Rel protein family. DFMO-induced NF-kappa B activation was accompanied by

the translocation of p65 from the cytoplasm into the nucleus. DFMO selectively inhibited a gene reporter construct dependent on the kappa B site present in the HLA-B7 gene. In contrast, DFMO had no effect on a gene reporter construct dependent on the kappa B site present in the interleukin-8 gene. Thus, we report that ODC inhibition activates the NF-kappa B transcription factor, which may mediate the altered physiological state of intestinal cells that occurs following polyamine depletion.

L9 ANSWER 2 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2001645880 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11697888
TITLE: Transglutaminase activity is involved in polyamine-induced programmed cell death.
AUTHOR: Facchiano F; D'Arcangelo D; Riccomi A; Lentini A; Beninati S; Capogrossi M C
CORPORATE SOURCE: Laboratorio di Patologia Vascolare, Istituto Dermopatico dell'Immacolata, Rome, Italy.. f.facchiano@idi.it
SOURCE: Experimental cell research, (2001 Nov 15) 271 (1) 118-29.
Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011108
Last Updated on STN: 20020123
Entered Medline: 20011227

AB Natural polyamines, i.e., putrescine, spermidine, and spermine, are ubiquitous molecules essential for cell proliferation and differentiation. In the present study, the effect of polyamines on primary cultures of bovine aortic endothelial cells (BAECs), rat aortic smooth muscle cells (RASMCs), and a human melanoma cell line was examined. While in the absence of fetal calf serum (FCS) polyamines had no effect on viability, in the presence of FCS spermidine and spermine, at concentrations close to physiologic levels, induced a dose-dependent cell death, whereas putrescine was ineffective. RASMCs were significantly more sensitive than other cells. FACS analysis, oligo-nucleosome ELISA, Hoechst nuclear staining, and Annexin V-FITC quantification showed that cell death was likely due to apoptosis. Cells exposed to spermidine showed a marked increase of intracellular transglutaminase (TGase) activity (approximately 30-fold over control). Inhibitors of polyamine oxidation or inhibitors of TGase activity **prevented polyamine**-induced **apoptosis**. Moreover, tissue TGase overexpression significantly increased cell sensitivity to polyamine, suggesting that this effect is likely related to enhanced intracellular TGase activity. These data indicate that polyamines may modulate cell viability through a novel TGase-dependent process.
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L9 ANSWER 3 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2001550263 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11598794
TITLE: Down-modulation of c-myc expression by phorbol ester protects CEM T leukaemia cells from starvation-induced apoptosis: role of ornithine decarboxylase and polyamines.
AUTHOR: Tiberio L; Maier J A; Schiaffonati L
CORPORATE SOURCE: Department of Biomedical Sciences and Biotechnology, University of Brescia, Via Valsabbina, 19, 25123 Brescia, Italy.
SOURCE: Cell death and differentiation, (2001 Oct) 8 (10) 967-76.
Journal code: 9437445. ISSN: 1350-9047.

PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011015
Last Updated on STN: 20020122
Entered Medline: 20011211

AB Myc is a transcriptional activator whose deregulated expression not only promotes proliferation but also induces or sensitizes cells to apoptosis. Here we demonstrate that c-myc plays a role in triggering apoptosis in CEM T leukaemia cells exposed to progressive medium exhaustion. Indeed starved cells undergo apoptosis in the presence of constitutively elevated c-myc expression and the phorbol ester, phorbol 12-myristate 13-acetate (PMA), which rescues cells from apoptosis, induces complete c-myc down-regulation. We also investigate the hypothesis that ornithine decarboxylase (ODC), a transcriptional target of c-myc, is a down-stream mediator of c-myc driven apoptosis. We demonstrate that PMA induces in starved cells an earlier and larger decrease in ODC expression (mRNA and activity) and intracellular polyamine content, compared to untreated starved cells. Moreover we show that alpha-difluoromethylornithine (DFMO), an irreversible inhibitor of ODC enzymatic activity, effectively **reduces**, while exogenous added **polyamines** enhance **apoptosis** in starved cells. All these data indicate that ODC and polyamines may act as facilitating factors in triggering apoptosis induced by growth/survival factors withdrawal.

L9 ANSWER 4 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2001478890 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11522638
TITLE: Apoptotic signaling in polyamine analogue-treated SK-MEL-28 human melanoma cells.
AUTHOR: Chen Y; Kramer D L; Diegelman P; Vujcic S; Porter C W
CORPORATE SOURCE: Grace Cancer Drug Center, Roswell Park Cancer Institute, Buffalo, New York 14263, USA.
CONTRACT NUMBER: CA16056 (NCI)
RO1 CA-22153 (NCI)
SOURCE: Cancer research, (2001 Sep 1) 61 (17) 6437-44.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010828
Last Updated on STN: 20010917
Entered Medline: 20010913

AB N(1),N(11)-Diethylnorspermine (DENSPM) is a polyamine analogue with clinical relevance as an experimental anticancer agent and the ability to elicit a profound apoptotic response in certain cell types. Here, we characterize the polyamine effects and apoptotic signaling events initiated by treatment of SK-MEL-28 human melanoma with 10 microm DENSPM. Maximal induction of the polyamine catabolic enzyme spermidine/spermine N(1)-acetyltransferase (SSAT) and polyamine pool depletion were seen by 16 h, whereas early apoptosis was first apparent at 36 h. Intermediate events related to apoptotic signaling were sought between 16 and 36 h. A loss of mitochondrial transmembrane potential ($\Delta\psi(m)$) beginning at 24 h was followed by the release of cytochrome c into the cytosol at 30 h. Loss of mitochondrial integrity was accompanied by caspase-3 activation and poly(ADP-ribose) polymerase digestion from 30 to 36 h. The caspase inhibitor Z-Asp-2,6-dichlorobenzoyloxymethylketone rendered cells resistant to analogue-induced caspase-3 activation and reduced the apoptotic response in a dose-dependent manner. Because polyamine reduction achieved by inhibitors of **polyamine** biosynthesis

inhibited growth but did not cause **apoptosis**, we looked for alternative **polyamine**-related events, focusing on induction of SSAT. Three DENSPM analogues that differentially induced SSAT activity but similarly depleted polyamine pools revealed a close correlation between enzyme induction and cytochrome c release, caspase activation, and apoptosis. Dose-dependent inhibition of polyamine oxidase, an enzyme that oxidizes acetylated polyamines generated by SSAT and releases toxic by-products such as H₂O₂ and aldehydes, prevented cytochrome c release, caspase activation, and apoptosis. Taken together, the findings indicate that DENSPM-induced apoptosis is at least partially initiated via massive induction of SSAT and related oxidative events and subsequently mediated by the mitochondrial apoptotic signaling pathway as indicated by cytochrome c release and caspase activation.

L9 ANSWER 5 OF 41 MEDLINE on STN
 ACCESSION NUMBER: 2001250697 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11346461
 TITLE: Troglitazone, a ligand for peroxisome proliferator-activated receptor gamma, inhibits chemically-induced aberrant crypt foci in rats.
 AUTHOR: Kohno H; Yoshitani S; Takashima S; Okumura A; Hosokawa M; Yamaguchi N; Tanaka T
 CORPORATE SOURCE: Department of Pathology, Kanazawa Medical University, Uchinada, Ishikawa 920-0293, Japan.
 SOURCE: Japanese journal of cancer research : Gann, (2001 Apr) 92 (4) 396-403.
 Journal code: 8509412. ISSN: 0910-5050.
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200107
 ENTRY DATE: Entered STN: 20010709
 Last Updated on STN: 20010709
 Entered Medline: 20010705

AB The biological roles of peroxisome proliferator-activated receptors (PPARs) in various diseases, including inflammation and cancer, have been highlighted recently. Although PPARGamma ligand is suspected to play an important role in carcinogenesis, its effects on colon tumorigenesis remain undetermined. The present time-course study was conducted to investigate possible modifying effects of a PPARGamma ligand, troglitazone, on the development and growth of aberrant crypt foci (ACF), putative precursor lesions for colon carcinoma, induced by azoxymethane (AOM) or dextran sodium sulfate (DSS) in male F344 rats. Oral troglitazone (10 or 30 mg / kg body weight (b.w.)) significantly reduced AOM (two weekly subcutaneous injections, 20 mg / kg b.w.)-induced ACF. Treatment with troglitazone increased apoptosis and decreased polyamine content and ornithine decarboxylase (ODC) activity in the colonic mucosa of rats treated with AOM. Gastric gavage of troglitazone also inhibited colitis and ACF induced by DSS (1% in drinking water), in conjunction with increased **apoptosis** and **reduced** colonic mucosal **polyamine** level and ODC activity. Our results suggest that troglitazone, a synthetic PPARGamma ligand, can inhibit the early stage of colon tumorigenesis with or without colitis.

L9 ANSWER 6 OF 41 MEDLINE on STN
 ACCESSION NUMBER: 2001112756 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11133803
 TITLE: Apoptosis induced by 1'-acetoxychavicol acetate in Ehrlich ascites tumor cells is associated with modulation of polyamine metabolism and caspase-3 activation.
 AUTHOR: Moffatt J; Hashimoto M; Kojima A; Kennedy D O; Murakami A; Koshimizu K; Ohigashi H; Matsui-Yuasa I
 CORPORATE SOURCE: Department of Food and Nutrition, Faculty of Human Life

SOURCE: Science, Osaka, City University, Osaka 558-8585, Japan.
Carcinogenesis, (2000 Dec) 21 (12) 2151-7.
Journal code: 8008055. ISSN: 0143-3334.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200102

ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010208

AB The efficacy of the antitumor activity of 1'-acetoxychavicol acetate (ACA), reported to be a suppressor of chemically induced carcinogenesis, was evaluated in Ehrlich ascites tumor cells. ACA treatment resulted in changes in morphology and a dose-dependent suppression of cell viability. Apoptosis, characterized by nuclear condensation, membrane blebbing, cell shrinkage and a significant induction of caspase-3-like protease activity at 8 h in a time-course study were observed. Formation of apoptotic bodies was preceded by lowering of intracellular polyamines, particularly putrescine, and both dose- and time-dependent inhibitory and activation effect by ACA on ornithine decarboxylase (ODC) and spermidine/spermine N(1)-acetyltransferase (SSAT), respectively. Administration of exogenous **polyamines prevented ACA-induced apoptosis** represented by a **reduction** in the number of apoptotic bodies and also caused reduction in the induced caspase-3-like protease activity at 8 h. These findings suggest that the anticarcinogenic effects of ACA might be partly due to perturbation of the polyamine metabolic pathway and triggering of caspase-3-like activity, which result in apoptosis.

L9 ANSWER 7 OF 41 MEDLINE on STN

ACCESSION NUMBER: 2000457117 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10712236

TITLE: Polyamine depletion delays apoptosis of rat intestinal epithelial cells.

AUTHOR: Ray R M; Viar M J; Yuan Q; Johnson L R

CORPORATE SOURCE: Department of Physiology, College of Medicine, University of Tennessee, Memphis, Memphis, Tennessee 38163, USA..
rray@physiol.utmem.edu

CONTRACT NUMBER: DK-16505 (NIDDK)

SOURCE: American journal of physiology. Cell physiology, (2000 Mar) 278 (3) C480-9.
Journal code: 100901225. ISSN: 0363-6143.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200009

ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005
Entered Medline: 20000922

AB The polyamines spermidine, spermine, and their precursor putrescine are essential for cell growth and the regulation of the cell cycle. Recent studies suggest that excessive accumulation of polyamines favors either malignant transformation or apoptosis, depending on the cell type and the stimulus. This study examines the involvement of **polyamines** in the induction of **apoptosis** by the DNA topoisomerase I **inhibitor**, camptothecin. In IEC-6 cells, camptothecin induced apoptosis within 6 h, accompanied by detachment of cells. Detached cells showed DNA laddering and caspase 3 induction, characteristic features of apoptosis. Depletion of putrescine, spermidine, and spermine by DL-alpha-difluoromethylornithine (DFMO), a specific inhibitor of ornithine decarboxylase (ODC) that is the first rate-limiting enzyme for polyamine biosynthesis, decreased the apoptotic index. Delayed apoptosis was accompanied by a decrease in caspase 3 activity in polyamine-depleted

cells. Addition of putrescine restored the induction of apoptosis as indicated by an increase in the number of detached cells and caspase 3 activity. Polyamine depletion did not change the level of caspase 3 protein. Inhibition of S-adenosylmethionine decarboxylase by a specific inhibitor [diethylglyoxal bis-(guanylhydrazone); DEGBG] led to depletion of spermidine and spermine with a significant accumulation of putrescine and induction of ODC. The DEGBG-treated cells showed an increase in apoptosis, suggesting the importance of putrescine in the apoptotic process. Addition of putrescine to DFMQ-treated cell extracts did not increase caspase 3 activity. The above results indicate that polyamine depletion delays the onset of apoptosis in IEC-6 cells and confers protection against DNA damaging agents, suggesting that polyamines might be involved in the caspase activating signal cascade.

L9 ANSWER 8 OF 41 MEDLINE on STN
 ACCESSION NUMBER: 2000453829 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11012080
 TITLE: Molecular correlates of the action of bis(ethyl)
polyamines in breast cancer cell growth
inhibition and apoptosis.
 AUTHOR: Faaland C A; Thomas T J; Balabhadrapathruni S; Langer T;
 Mian S; Shirahata A; Gallo M A; Thomas T
 CORPORATE SOURCE: Department of Environmental and Community Medicine,
 Environmental and Occupational Health Sciences Institute,
 University of Medicine and Dentistry of New Jersey-Robert
 Wood Johnson Medical School, New Brunswick 08903, USA.
 CONTRACT NUMBER: ES05022 (NIEHS)
 RO1 CA42439 (NCI)
 RO1 CA73058 (NCI)
 SOURCE: Biochemistry and cell biology = Biochimie et biologie
 cellulaire, (2000) 78 (4) 415-26.
 Journal code: 8606068. ISSN: 0829-8211.
 PUB. COUNTRY: Canada
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200101
 ENTRY DATE: Entered STN: 20010322
 Last Updated on STN: 20010322
 Entered Medline: 20010118
 AB Polyamines are known to be involved in cell growth regulation in breast
 cancer. To evaluate the efficacy of bis(ethyl)polyamine analogs for
 breast cancer therapy and to understand their mechanism of action we
 measured the effects of a series of polyamine analogs on cell growth,
 activities of enzymes involved in polyamine metabolism, intracellular
 polyamine levels, and the uptake of putrescine and spermidine using MCF-7
 breast cancer cells. The IC50 values for cell growth inhibition of three
 of the compounds, N1,N12-bis(ethyl)spermine, N1,N11-bis(ethyl)norspermine,
 and N1,N14-bis(ethyl)homospermine, were in the range of 1-2 microM.
 Another group of three compounds showed antiproliferative activity at
 about 5 microM level. These compounds are also capable of suppressing
 colony formation in soft agar assay and inducing apoptosis of MCF-7 cells.
 The highly effective growth inhibitory agents altered the activity of
 polyamine biosynthetic and catabolic enzymes and down-regulated the
 transport of natural polyamines, although each compound produced a unique
 pattern of alterations in these parameters. HPLC analysis showed that
 cellular uptake of bis(ethyl)polyamines was highest for
 bis(ethyl)spermine. We also analyzed polyamine analog conformations and
 their binding to DNA minor or major grooves by molecular modelling and
 molecular dynamics simulations. Results of these analyses indicate that
 tetramine analogs fit well in the minor groove of DNA whereas, larger
 compounds extend out of the minor groove. Although major groove binding
 was also possible for the short tetramine analogs, this interaction led to
 a predominantly bent conformation. Our studies show growth inhibitory

activities of several potentially important analogs on breast cancer cells and indicate that multiple sites are involved in the mechanism of action of these analogs. While the activity of an analog may depend on the sum of these different effects, molecular modelling studies indicate a correlation between antiproliferative activity and stable interactions of the analogs with major or minor grooves of DNA.

L9 ANSWER 9 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2000420099 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10920982
TITLE: Cloning and expression of a gene associated with HL60 cell
apoptosis induced by **inhibition** of
polyamine biosynthesis.
AUTHOR: Feng L; Fan M
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology,
China-Japan Friendship Institute of Clinical Medical
Sciences, Beijing.
SOURCE: Zhonghua zhong liu za zhi [Chinese journal of oncology],
(1998 Jul) 20 (4) 274-6.
Journal code: 7910681. ISSN: 0253-3766.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000915
Last Updated on STN: 20000915
Entered Medline: 20000906

AB OBJECTIVE: To clone the gene associated with **apoptosis** induced
by an **inhibitor** of **polyamine** biosynthesis,
alpha-difluoromethylornithine (DFMO). METHODS: The differential
substraction screening was used for gene cloning. The gene expression and
apoptosis of transfected HL60 cells were detected by Northern blot,
morphological assay, FCM and ladder map of DNA electrophoresis,
respectively. RESULTS: An apoptosis-associated gene named dF4 was cloned
from HL60 cells treated with polyamine biosynthesis inhibitor. The
programmed cell death was demonstrated in the HL60 cells transfected by
dF4 gene. CONCLUSION: dF4 gene cloned in this study could be a gene
regulating apoptosis of HL60 cells.

L9 ANSWER 10 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2000075377 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10607308
TITLE: alpha-Difluoromethylornithine blocks thymocyte apoptosis
via a reduction in tyrosine phosphorylation.
AUTHOR: Jan M S; Wing L Y; Lin M T; Lin Y S
CORPORATE SOURCE: Departments of Microbiology and Immunology, Physiology and
Biochemistry, National Cheng Kung University Medical
College, Tainan, Taiwan, Republic of China.
SOURCE: Scandinavian journal of immunology, (1999 Dec) 50
(6) 605-11.
Journal code: 0323767. ISSN: 0300-9475.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000124
Last Updated on STN: 20000124
Entered Medline: 20000111

AB The effect of alpha-difluoromethylornithine on cell apoptosis was
investigated. Freshly isolated mouse thymocytes were cultured in the
medium alone or with dexamethasone, and apoptotic cell death was monitored
after 6 h. A correlation was seen between cell **apoptosis** and a

reduction in the **polyamine** levels of thymocytes. Addition of exogenous polyamines decreased the levels of apoptosis induced spontaneously in the culture medium or by dexamethasone. However, addition of alpha-difluoromethylornithine, an irreversible inhibitor of ornithine decarboxylase, to the cultures did not enhance apoptosis but rather caused inhibition of thymocyte apoptosis. Analysis of the mechanism of alpha-difluoromethylornithine-mediated inhibition of apoptosis indicated that alpha-difluoromethylornithine treatment blocked protein tyrosine phosphorylation, which was elevated drastically during the first hour of thymocyte cultivation. Treatment with the phosphotyrosine phosphatase inhibitor phenylarsine oxide reversed this inhibitory effect of alpha-difluoromethylornithine on apoptotic cell death. Our results provide an alternative mechanism for alpha-difluoromethylornithine showing the inhibition of apoptosis via reduction of protein tyrosine phosphorylation.

L9 ANSWER 11 OF 41 MEDLINE on STN
 ACCESSION NUMBER: 1999446897 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10519408
 TITLE: The **polyamine** oxidase inhibitor
 MDL-72,527 selectively induces **apoptosis** of
 transformed hematopoietic cells through lysosomotropic
 effects.
 AUTHOR: Dai H; Kramer D L; Yang C; Murti K G; Porter C W; Cleveland
 J L
 CORPORATE SOURCE: Department of Biochemistry, St. Jude Children's Research
 Hospital, Memphis, Tennessee 38105, USA.
 CONTRACT NUMBER: CA21765 (NCI)
 CA22153 (NCI)
 DK44158 (NIDDK)
 SOURCE: Cancer research, (1999 Oct 1) 59 (19) 4944-54.
 Journal code: 2984705R. ISSN: 0008-5472.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199911
 ENTRY DATE: Entered STN: 20000111
 Last Updated on STN: 20021210
 Entered Medline: 19991104

AB Polyamine oxidase functions in the polyamine catabolic pathway, converting N1-acetyl-spermidine and -spermine into putrescine (Put) and spermidine (Spd), respectively, thereby facilitating homeostasis of intracellular polyamine pools. Inhibition of polyamine oxidase in hematopoietic cells by a specific inhibitor, N,N'-bis(2,3-butadienyl)-1,4-butanediamine (MDL-72,527), reduces the levels of Put and Spd and induces the accumulation of N1-acetylated Spd. Although previously thought to be relatively nontoxic, we now report that this inhibitor overrides survival factors to induce cell death of several immortal and malignant murine and human hematopoietic cells, but not of primary myeloid progenitors. Cells treated with MDL-72,527 displayed biochemical changes typical of apoptosis, and cell death was associated with the down-regulation of the antiapoptotic protein Bcl-X(L). However, enforced overexpression of Bcl-X(L), or treatment with the universal caspase inhibitor zVAD-fmk, failed to block MDL-72,527-induced apoptosis in these hematopoietic cells. Despite decreases in Put and Spd pools, MDL-72,527-induced apoptosis was not blocked by cotreatment with exogenous Put or Spd, nor was it influenced by overexpression or inhibition of the polyamine biosynthetic enzyme ornithine decarboxylase. Significantly, MDL-72,527-induced apoptosis was associated with the rapid formation of numerous lysosomally derived vacuoles. Malignant leukemia cells were variably sensitive to the lysosomotropic effects of MDL-72,527, yet pretreatment with the ornithine decarboxylase inhibitor L-alpha-difluoromethylornithine sensitized all of these leukemia cells to the deleterious effects of the inhibitor by

stimulating its intracellular accumulation. The lysosomotropic nature of select polyamine analogues may, thus, provide a novel chemotherapeutic strategy to selectively induce apoptosis of malignant hematopoietic cells.

L9 ANSWER 12 OF 41 MEDLINE on STN
ACCESSION NUMBER: 1999200678 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10102555
TITLE: **Polyamines** found in the inflamed periodontium
inhibit priming and **apoptosis** in human
polymorphonuclear leukocytes.
AUTHOR: Ratasirayakorn W; Leone P; Leblebicioglu B; Walters J D
CORPORATE SOURCE: Section of Periodontology, College of Dentistry, The Ohio
State University Health Sciences Center, Columbus 43210,
USA.
CONTRACT NUMBER: K04 DE00338 (NIDCR)
ROI DE09851 (NIDCR)
SOURCE: Journal of periodontology, (1999 Feb) 70 (2)
179-84.
Journal code: 8000345. ISSN: 0022-3492.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990601
Last Updated on STN: 20000303
Entered Medline: 19990517
AB BACKGROUND: Polymorphonuclear leukocytes (PMNs) are exposed to high
concentrations of polyamines in the inflamed periodontium and possess a
transport system for taking up these compounds. Previous studies suggest
that polyamines are involved in priming of the PMN respiratory burst by
tumor necrosis factor-alpha (TNF-alpha) and can stabilize DNA against
degradation. The purpose of this study was to determine whether exogenous
polyamines can modulate priming by TNF-alpha or delay nuclear changes
associated with PMN apoptosis (programmed cell death). METHODS: Isolated
human PMNs were incubated with putrescine or spermidine in vitro.
Superoxide generation was measured with a cytochrome C reduction assay,
and apoptotic changes were assessed by fluorescence microscopy (after cell
staining with acridine orange and ethidium bromide). RESULTS: Incubation
with 1 mM putrescine for 1 hour inhibited superoxide production by
TNF-primed PMNs by 20%, but enhanced the production of superoxide by
unprimed cells by 38%. Both effects were dose dependent and statistically
significant (P <0.03, repeated measures ANOVA and Dunnett's test).
Spermidine had no significant effects on PMN oxidative function. With
regard to apoptosis, 1 mM putrescine or spermidine produced a
statistically significant reduction in the proportion of apoptotic PMNs
within 6 to 9 hours (P <0.05). In cells incubated for 7 hours with 300
microM putrescine or spermidine, the proportion of apoptotic cells was
approximately 30% lower than in untreated controls (P <0.05, Dunnett's
test). The delay of apoptosis by spermidine was less profound than that
produced by TNF-alpha and was not additive to the effects of this
cytokine. CONCLUSIONS: Polyamines could potentially impair the priming of
PMN oxidative function by TNF-alpha at sites where this cytokine is
present. In the absence of TNF-alpha, polyamines could enhance PMN
superoxide release and enhance the maintenance of PMN function in the
periodontal pocket.

L9 ANSWER 13 OF 41 MEDLINE on STN
ACCESSION NUMBER: 1998444792 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9773808
TITLE: Mitoguazone induces apoptosis via a p53-independent
mechanism.
AUTHOR: Davidson K; Petit T; Izbicka E; Koester S; Von Hoff D D
CORPORATE SOURCE: Institute for Drug Development, Cancer Therapy & Research

Center and the University of Texas Health Science Center at
San Antonio, 78229, USA.

SOURCE: Anti-cancer drugs, (1998 Aug) 9 (7) 635-40.
Journal code: 9100823. ISSN: 0959-4973.

PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199812

ENTRY DATE: Entered STN: 19990115

Last Updated on STN: 19990115

Entered Medline: 19981215

AB Mitoguazone (methylglyoxal bisguanylhydrazone, methyl-GAG or MGBG) is a synthetic polycarbonyl derivative with activity in patients with Hodgkin's and non-Hodgkin's lymphoma, head and neck cancer, prostate cancer, and esophageal cancer. Mitoguazone has also recently been documented to have activity in patients with AIDS-related lymphoma. Among anticancer drugs, mitoguazone has a unique mechanism of action via interference with the polyamine biosynthetic pathway. Polyamines stabilize DNA structure by non-covalent cross-bridging between phosphate groups on opposite strands. In addition, mitoguazone causes uncoupling of oxidative phosphorylation. In this study, the ability of mitoguazone to induce **apoptosis** by **inhibiting** the **polyamine** pathway was assessed in three Burkitt's lymphoma cell lines (Raji, Ramos and Daudi) and one prostate carcinoma cell line (MPC 3). Additional evaluations were performed in two human breast cancer cell lines (MCF7 with wild-type p53 and VM4K with mutated p53) to determine whether the p53 tumor suppressor gene was required for efficient apoptosis induction. The present study demonstrated that mitoguazone induces apoptosis in all the different human cancer cell lines tested in a concentration- and time-dependent way, and triggers a p53-independent programmed cell death in the human breast cancer MCF7 cell line.

L9 ANSWER 14 OF 41 MEDLINE on STN

ACCESSION NUMBER: 1998297958 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9632528

TITLE: Sensitization of tn timer-induced **apoptosis** with
polyamine synthesis **inhibitors** in
different human and murine tumour cell lines.

AUTHOR: Penning L C; Schipper R G; Vercammen D; Verhofstad A A;
Denecker T; Beyaert R; Vandenabeele P

CORPORATE SOURCE: Laboratory of Molecular Biology, University of Gent,
Flemish Interuniversity Institute of Biotechnology, K.L.
Ledeganckstraat 35, B-9000 Gent, Belgium.. lopen@sci.kun.nl

SOURCE: Cytokine, (1998 Jun) 10 (6) 423-31.
Journal code: 9005353. ISSN: 1043-4666.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199807

ENTRY DATE: Entered STN: 19980723

Last Updated on STN: 19980723

Entered Medline: 19980715

AB Rat/mouse T cell hybridoma-derived PC60 R55/R75 cells were used as a model to study tumour necrosis factor (TNF)-induced apoptosis. The role of ornithine decarboxylase (ODC) activity and polyamines in this process was investigated. In PC60 R55/R75 cells, TNF-induced ODC activity was completely suppressed by externally added spermine (Spm). TNF decreased the intracellular levels of the three polyamines Spm, spermidine (Spd) and putrescine (Put). A reduction of the intracellular [Spm] with methylglyoxal bis(quanyl hydrazones) (MGBG), CGP48644a, or bis(ethyl)norspermine (BENSpm), clearly sensitized the cells towards the apoptotic effect of TNF. Conversely, an increase in intracellular [Spm]

with DFMO or externally added Spm reduced cellular sensitivity. Similar results were obtained after TNF treatment of the human cell lines Kym 39A6 (rhabdomyosarcoma), HeLaH21 (cervix carcinoma) and U937 (histiocytoma) and after alphaFas treatment of HeLaH21, U937 and CEM-CM3 (human T cell line). These results suggest that a decrease of intracellular Spm levels rather than ODC activity per se is involved in the sensitization towards apoptosis induced by TNF or alphaFas.

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L9 ANSWER 15 OF 41 MEDLINE on STN
ACCESSION NUMBER: 97357274 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9214603
TITLE: Involvement of polyamines in selenomethionine induced apoptosis and mitotic alterations in human tumor cells.
AUTHOR: Redman C; Xu M J; Peng Y M; Scott J A; Payne C; Clark L C; Nelson M A
CORPORATE SOURCE: Pharmacology/Toxicology Department, The Arizona Cancer Center, The University of Arizona, Tucson 85724, USA.
CONTRACT NUMBER: CA41108-MIS (NCI)
CA49764 (NCI)
R29 CA70145-01 (NCI)
+
SOURCE: Carcinogenesis, (1997 Jun) 18 (6) 1195-202.
Journal code: 8008055. ISSN: 0143-3334.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970812
Last Updated on STN: 19970812
Entered Medline: 19970725

AB The efficacy of dietary selenium supplementation is currently being evaluated in intervention trials. However, the biological mechanisms underlying the cancer chemopreventive effects of selenium supplementation have yet to be elucidated. Selenium metabolism and polyamine biosynthesis are linked in their common requirement for S-adenosylmethionine. Selenomethionine was the predominant form of selenium in the dietary supplement, therefore we evaluated the anti-tumorigenic effects of selenomethionine. We found that selenomethionine inhibited tumor growth (both in A549 lung and HT29 colon cancer cells) in a dose-dependent manner. At 24 and 72 h, polyamine content of A549 and HT29 cancer cell lines was decreased at doses that inhibited 50% of normal growth. Selenomethionine treatment induced apoptosis in both cancer cell lines. Exogenous spermine administration, which replenishes intracellular **polyamine** levels, **prevented** selenomethionine induced **apoptosis**. Selenomethionine administration to the cancer cell lines increased the number of cells in metaphase. This cell cycle effect appeared to be reversed with the co-administration of selenomethionine and spermine. These data suggested that at least part of the anti-carcinogenic effects of selenium supplementation might be due to a depletion in polyamine levels. This depletion of polyamines leads to an induction in apoptosis and perturbations in the cell cycle.

L9 ANSWER 16 OF 41 MEDLINE on STN
ACCESSION NUMBER: 97270327 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9125410
TITLE: Polyamines prevent apoptotic cell death in cultured cerebellar granule neurons.
AUTHOR: Harada J; Sugimoto M
CORPORATE SOURCE: Neuroscience Research Laboratories, Sankyo Co. Ltd., Shinagawa-ku, Tokyo, Japan.. jyunha@shina.sankyo.co.jp
SOURCE: Brain research, (1997 Apr 11) 753 (2) 251-9.
Journal code: 0045503. ISSN: 0006-8993.

PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970709
Last Updated on STN: 20000303
Entered Medline: 19970623

AB Polyamines play critical roles during the development of brain neurons. In the present study we examined the effects of polyamines on neuronal apoptotic death. Rat cerebellar granule neurons were cultured in the presence of a depolarizing concentration of KCl (25 mM) in the medium. Apoptotic neuronal death was induced by changing the medium to that containing 5.6 mM KCl without serum. Spermine as well as spermidine and putrescine prevented cell death in a concentration-dependent manner with the order of potency being spermine > spermidine > putrescine. The effect of spermine was partially blocked by several NMDA-type glutamate receptor antagonists including (+)-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5,10-imine (MK-801). MK-801-sensitive neuroprotection by spermine depended on cell density. Activation of CPP32 (caspase-3/Yama/apopain)-like proteolytic activity, a key mediator of **apoptosis**, precedes neuronal death, and **polyamines prevented** an increase in this activity. These results demonstrate that polyamines protect neurons from apoptotic cell death through both NMDA receptor-dependent and -independent mechanisms, acting upstream from the activation of CPP32-like protease(s).

L9 ANSWER 17 OF 41 MEDLINE on STN
ACCESSION NUMBER: 95074065 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7982974
TITLE: Different prooxidant levels stimulate growth, trigger apoptosis, or produce necrosis of insulin-secreting RINm5F cells. The role of intracellular polyamines.
AUTHOR: Dypbukt J M; Ankarcrona M; Burkitt M; Sjöholm A; Strom K; Orrenius S; Nicotera P
CORPORATE SOURCE: Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden.
SOURCE: Journal of biological chemistry, (1994 Dec 2) 269 (48) 30553-60.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950116
Last Updated on STN: 19980206
Entered Medline: 19941230

AB Increasing concentrations (1-100 microM) of the redox cycling quinone, 2,3-dimethoxy-1,4-naphthoquinone (DMNQ), stimulated growth, triggered apoptosis, or caused necrosis of pancreatic RINm5F cells, depending on the dose and duration of the exposure. Following the exposure of RINm5F cells to 10 microM DMNQ, ornithine decarboxylase activity and polyamine biosynthesis increased. This was accompanied by enhanced cell proliferation. Conversely, exposure to 30 microM DMNQ for 3 h resulted in the inhibition of ornithine decarboxylase, intracellular polyamine depletion, and apoptotic cell killing. Pretreatment of the cultures with the phorbol ester, 12-O-tetradecanoylphorbol-13-acetate, restored **polyamine** levels and **prevented apoptosis**. Exposure to the same DMNQ concentration for only 1 h, with subsequent re-incubation in growth medium, neither caused polyamine depletion nor resulted in apoptosis. Finally, exposure to an even higher DMNQ concentration (100 microM) for either 1 or 3 h caused rapid intracellular Ca²⁺ overload, ATP, NAD⁺, and glutathione depletion, and extensive DNA

single strand breakage, which resulted in necrotic cell death. Our results show that a disturbance of polyamine biosynthesis occurred prior to cell growth or apoptosis elicited by oxidative stress. In addition, we show that effects as opposite as cell proliferation and deletion, by either apoptosis or necrosis, can be induced, in the same system, by varying the exposure to a prooxidant.

L9 ANSWER 18 OF 41 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:576082 BIOSIS

DOCUMENT NUMBER: PREV200100576082

TITLE: Induction of apoptosis in human gastric cancer cell lines by the polyamine synthesis inhibitor, methylglyoxal bis(cyclopentylamidinohydrazone) (MGBCP).

AUTHOR(S): Nakashima, S.; Hibasami, H. [Reprint author]; Tamaki, S.; Toyota, N.; Taguchi, Y.; Yamaguchi, M.; Gabazza, E. C.; Ikoma, J.; Kaito, M.; Imoto, I.; Nakashima, K.; Adachi, Y.

CORPORATE SOURCE: Faculty of Medicine, Department of Medical Sciences, Mie University, 2-174 Edobashi, Tsu-city, Mie, 514-8507, Japan

SOURCE: Biogenic Amines, (2001) Vol. 16, No. 4-5, pp. 327-342.

print.

CODEN: BIAME7. ISSN: 0168-8561.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 12 Dec 2001

Last Updated on STN: 25 Feb 2002

AB Polyamines are important intracellular mediators of cell proliferation in cancer cells. In this study, we evaluated whether methylglyoxal bis(cyclopentylamidinohydrazone) (MGBCP), a **polyamine** synthesis **inhibitor**, induces **apoptosis** and **inhibits** growth in gastric cancer cell lines (MKN-1, MKN-28, MKN-45). For comparison, the same experiment was carried out in a normal rat gastric epithelial cell line (RGM-1). The growth of gastric cancer cell lines was dose-dependently inhibited by MGBCP. Almost all the cells became apoptotic when they were cultured in the presence of 40 μ M MGBCP for 5 days. Very high concentration (200 μ M) of MGBCP was needed to completely inhibit the proliferation of RGM-1 cells. The cellular concentrations of the polyamines, spermidine and spermine were significantly reduced (50%) when the gastric cancer cells were cultured in the presence of MGBCP (80 μ M) for 5 days. Putrescine remained unchanged. The reductions of both spermidine and spermine were mild in RGM-1 cells. DNA fragmentation and TUNEL studies demonstrated the occurrence of apoptosis in gastric cancer cell lines but not in RGM-1 cells. The results of this study suggest the potential usefulness of MGBCP as an anti-cancer agent in gastric cancer.

L9 ANSWER 19 OF 41 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:275600 BIOSIS

DOCUMENT NUMBER: PREV200100275600

TITLE: Polyamine depletion inhibits growth and induces inhibitors of the cell cycle in primary cultures of human uterine leiomyomas.

AUTHOR(S): Broadus, Russell Ray [Reprint author]; Xie, Susu [Reprint author]; Zou, Changping

CORPORATE SOURCE: University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX, 77030-4009, USA

SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1181. print.

Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001. Orlando, Florida, USA. March 31-April 04, 2001.

CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 6 Jun 2001

Last Updated on STN: 19 Feb 2002

AB Background: Uterine leiomyomas, smooth muscle tumors of the uterus, are a major cause of infertility and dysfunctional uterine bleeding. Leiomyomas are the most common indication for hysterectomy in the U.S. Despite their prevalence, relatively little is known of the factors that control leiomyoma growth. It is our long-term objective to dissect the pathways important in leiomyoma growth regulation so that non-surgical therapies can be developed. For the present study, we examined the effects of DFMO, an inhibitor of ornithine decarboxylase and polyamine synthesis, on primary cultures of human uterine leiomyomas. Design: Primary cell cultures of human uterine leiomyomas and normal myometrium were established from fresh hysterectomy specimens and then incubated with DFMO (1mM). The cultures were examined for growth inhibition and apoptosis via flow cytometric TUNEL analysis. The cell cycle regulatory proteins p53, p21, and p16 were analyzed by Western blotting of leiomyoma cell lysates following DFMO treatment. Results: DFMO treatment caused significant growth inhibition of leiomyoma cell growth, but had no effect on normal myometrial cells. Maximal growth inhibition was seen at 4-5 days following the addition of DFMO. Growth inhibition was also associated with apoptosis. Polyamine depletion induced overexpression of p53, p21, and p16, beginning 5 days after exposure to DFMO. Conclusions: These results indicate that polyamines are an important mediator of leiomyoma cell growth. DFMO, an inhibitor of **polyamine** synthesis, causes growth **inhibition, apoptosis**, and the induction of the negative regulatory proteins p53, p21, and p16 in leiomyoma cells. The effects of DFMO appear to be selective, as normal myometrial cells are not affected.

L9 ANSWER 20 OF 41 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:192674 BIOSIS
DOCUMENT NUMBER: PREV199900192674
TITLE: **Polyamine** depletion **prevents**
etoposide-induced **apoptosis** in human leukemic
cells.
AUTHOR(S): Lindsay, G. S.; Wallace, H. M.
CORPORATE SOURCE: Univ. Aberdeen, Aberdeen AB25 2ZD, UK
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (March, 1999) Vol. 40, pp. 322. print.
Meeting Info.: 90th Annual Meeting of the American
Association for Cancer Research. Philadelphia,
Pennsylvania, USA. April 10-14, 1999. American Association
for Cancer Research.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1999
Last Updated on STN: 5 May 1999

L9 ANSWER 21 OF 41 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1996:480214 BIOSIS
DOCUMENT NUMBER: PREV199699195470
TITLE: Inhibitory role of polyamines in dexamethasone-induced
apoptosis of mouse thymocytes.
AUTHOR(S): Choi, Sang-Hyun; Kim, Yong-Hoon; Hong, Gi-Hyun; Shin,
Kyung-Ho; Chun, Yeon-Sook; Chun, Boe-Gwun [Reprint author]
CORPORATE SOURCE: Dep. Pharmacol., Korea Univ. Coll. Med., Seoul 136-705,
South Korea
SOURCE: Korean Journal of Pharmacology, (1996) Vol. 32, No. 1, pp.
113-123.
CODEN: KJPHE3. ISSN: 0377-9459.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Oct 1996

Last Updated on STN: 24 Oct 1996

AB It has been well known that polyamines ensure the stability of chromatin structure and the fidelity of DNA transcription. This study was carried out to evaluate the effect of polyamines on the apoptosis of mouse thymocytes induced by dexamethasone and polyamine synthesis inhibitors. 1) In the histological death findings of thymocytes double-stained with acridine orange and ethidium bromide, the apoptotic and the necrotic fractions (AF; NF) in the control group were 9.4+-4.2% and 4.5+-5.3%, respectively. Dexamethasone (3 times 10-8 M: DX) increased AF upto 52.0+-8.1% and did not change NF, but A23187 (5 times 10-7 M: A2) increased AF and NF upto 45.0+-8.9% and 20.5+-10.6%, respectively. 2) The thymocyte viability was significantly reduced by DX, DHEA (1 times 10-4 M), A2, DFMO (1 times 10-4 M), and MGBG (1 times 10-4 M), respectively. It was, however, little affected by aminoguanidine (1 times 10-4 M: AG), putrescine (1 times 10-5 M: PT), spermidine (1 times 10-3 M: SD), and spermine (1 times 10-5 M: SM). 3) The genomic DNA of mouse thymocyte was markedly fragmented by DX and A2, respectively, and to a lesser extent, by DHEA, but was little affected by MGBG, DFMO, AG, and each of polyamines. 4) The DX induced reduction of thymocyte viability was moderately attenuated by DHEA, but little affected by DFMO, MGBG, and AG. However, SM significantly attenuated the viability reduction induced by A2 as well as DX. 5) The thymocyte viability reduction by MGBG and DFMO was significantly attenuated by only SM among three polyamines applied in this study. 6) The thymocyte viability reduction by combined treatments of DX with DFMO and MGBG, respectively, was significantly attenuated by SM, and moderately by PT. But the viability reduction by combined treatment of DX with AG or DHEA was not affected by polyamines. These results suggest that **polyamines**, particularly spermine, might play the **inhibitory** role in thymocyte **apoptosis** and the inhibitory effect can be ascribed in part to the increase of polyamine uptake by thymocytes pretreated with DFMO and MGBG.

L9 ANSWER 22 OF 41 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1992:364244 BIOSIS
DOCUMENT NUMBER: PREV199243042394; BR43:42394
TITLE: CHLORODEOXYADENOSINE TOXICITY IN HAIRY CELL LEUKEMIA
EFFECTS OF PHORBOL ESTER AND **POLYAMINE** SYNTHESIS
INHIBITORS ON APOPTOSIS.
AUTHOR(S): CARRERA C J [Reprint author]; PIRO L D; SAVEN A; BEUTLER E;
CARSON D A
CORPORATE SOURCE: UNIV CALIF, SAN DIEGO, CALIF 92093, USA
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (1992) Vol. 33, pp. 150.
Meeting Info.: 83RD ANNUAL MEETING OF THE AMERICAN
ASSOCIATION FOR CANCER RESEARCH, SAN DIEGO, CALIFORNIA,
USA, MAY 20-23, 1992. PROC AM ASSOC CANCER RES ANNU MEET.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 30 Jul 1992
Last Updated on STN: 30 Jul 1992

L9 ANSWER 23 OF 41 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 1999254130 EMBASE
TITLE: Cloning and expression of a gene associated with HL60 cell
apoptosis induced by **inhibition** of
polyamine biosynthesis.
AUTHOR: Feng L.; Fan M.
CORPORATE SOURCE: M. Fan, Dept. of Biochemistry/Molec. Biology, China-Japan
Friendship Institute, Clinical Medical Sciences, Hepingli
Street, Beijing 100029, China. muzhfan@public.eastcn.net
SOURCE: Chinese Journal of Cancer Research, (1999) 11/2 (88-91).

Refs: 8
 ISSN: 1000-9604 CODEN: CJCRFH
 COUNTRY: China
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 016 Cancer
 022 Human Genetics
 025 Hematology
 029 Clinical Biochemistry
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB Objective: To done the gene associated with **apoptosis** induced by an **inhibitor** of **polyamine** biosynthesis, α -difluoromethylornithine (DFMO). Methods: The differential subtraction screening was used for gene cloning from cDNA library of HL60 cells treated by DFMO. Northern blot, morphological observation, FCM assays and ladder map of DNA electrophoresis were performed. Results: The transfecting gene expression and activity of inducing apoptosis in the cells transfected from recombinant plasmid containing the cloned fragment df4 was proved. Conclusion: It is suggest that df4 gene cloned in the study could be a gene regulating apoptosis of HL60 cells.

L9 ANSWER 24 OF 41 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
 on STN

ACCESSION NUMBER: 1998341334 EMBASE
 TITLE: Inhibition of proteasome function prevents thymocyte apoptosis: Involvement of ornithine decarboxylase.
 AUTHOR: Grassilli E.; Benatti F.; Dansi P.; Giammarioli A.M.; Malorni W.; Franceschi C.; Desiderio M.A.
 CORPORATE SOURCE: M.A. Desiderio, Institute of General Pathology, University of Milan, via L. Mangiagalli 31, 20133 Milan, Italy. desi@imiucca.csi.unimi.it
 SOURCE: Biochemical and Biophysical Research Communications, (18 Sep 1998) 250/2 (293-297).
 Refs: 34
 ISSN: 0006-291X CODEN: BBRCA
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 029 Clinical Biochemistry
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB We have previously shown that polyamine levels rapidly decrease in thymocytes undergoing apoptosis, and that ornithine decarboxylase increases early but too transiently to maintain elevated polyamine levels. These data led us to suppose that a precocious ornithine decarboxylase degradation might be responsible for the imbalance of polyamine metabolism. Ornithine decarboxylase is known to be degraded by the cytosolic 26S proteasome that plays an essential role in thymocyte apoptosis. In this paper we demonstrate that the inhibition of proteasome function preserves ornithine decarboxylase activity and **prevents** thymocytes from undergoing **apoptosis** after dexamethasone treatment. Since intracellular **polyamine** levels are also preserved, ornithine decarboxylase seems to be functionally active in maintaining polyamine homeostasis after proteasome inhibition in thymocytes. Our proposed role for the proteasome in quiescent cells upon an apoptotic stimulus is to degrade proteins like ornithine decarboxylase that are involved in the control of the cell cycle and cell survival.

L9 ANSWER 25 OF 41 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
 on STN

ACCESSION NUMBER: 1998001039 EMBASE
 TITLE: Excess putrescine accumulation inhibits the formation of modified eukaryotic initiation factor 5A (eIF-5A) and induces apoptosis.
 AUTHOR: Tome M.E.; Fiser S.M.; Payne C.M.; Gerner E.W.

CORPORATE SOURCE: E.W. Gerner, Department of Radiation Oncology, Arizona Health Sciences Center, University of Arizona, Tucson, AZ 85724

SOURCE: Biochemical Journal, (1997) 328/3 (847-854).
Refs: 62

ISSN: 0264-6021 CODEN: BIJOAK

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB DH23A cells, an α -difluoromethylornithine-resistant variant of the parental hepatoma tissue culture cells, express high levels of stable ornithine decarboxylase. Aberrantly high expression of ornithine decarboxylase results in a large accumulation of endogenous putrescine and increased apoptosis in DH23A cells when α -difluoromethylornithine is removed from the culture. Treatment of DH23A cells with exogenous putrescine in the presence of α -difluoromethylornithine mimics the effect of drug removal, suggesting that putrescine is a causative agent or trigger of **apoptosis**. Accumulation of excess intracellular **putrescine inhibits** the formation of hypusine in vivo, a reaction that proceeds by the transfer of the butylamine moiety of spermidine to a lysine residue in eukaryotic initiation factor 5A (eIF-5A). Treatment of DH23A cells with diaminoheptane, a competitive inhibitor of the post-translational modification of eIF-5A, causes both the suppression of eIF-5A modification in vivo and induction of apoptosis. These data support the hypothesis that rapid degradation of ornithine decarboxylase is a protective mechanism to avoid cell toxicity from putrescine accumulation. Further, these data suggest that suppression of modified eIF-5A formation is one mechanism by which cells may be induced to undergo apoptosis.

L9 ANSWER 26 OF 41 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 97384108 EMBASE

DOCUMENT NUMBER: 1997384108

TITLE: Anti-IgM-induced growth inhibition and apoptosis are independent of ornithine decarboxylase in Ramos cells.

AUTHOR: Lin C.-K.E.; Zou H.Y.; Kaptein J.S.; Yen C.F.; Kalunta C.I.; Tam Thuan Nguyen; Park E.; Lad P.M.

CORPORATE SOURCE: P.M. Lad, Regional Research Laboratory, Kaiser Foundation Hospitals, 1515 N. Vermont Ave, Los Angeles, CA 90027, United States

SOURCE: Experimental Cell Research, (1997) 237/1 (231-241).

Refs: 59

ISSN: 0014-4827 CODEN: ECREAL

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Ornithine decarboxylase (ODC) is a key enzyme involved in polyamine production and is thought to regulate growth and apoptosis in multiple cell systems. A potential link between ODC and growth may involve the action of an oncogene c-myc which is thought to transcriptionally regulate ODC. We have examined the involvement of ODC in anti-IgM-induced growth inhibition and apoptosis in Burkitt's lymphoma cells. Inhibitors of ODC such as difluoromethylornithine (DFMO) completely blocked ODC activity, resulting in growth **inhibition** but not **apoptosis**. Addition of **putrescine**, the product of ODC enzymatic action, to Ramos cells had only a minor effect on growth, did not cause apoptosis, did not augment or block anti-IgM-mediated growth inhibition and apoptosis, but did reverse DFMO-mediated growth inhibition. Anti-IgM treatment of Ramos cells, which markedly decreased c-myc mRNA and protein,

caused a paradoxical increase in ODC mRNA level as well as ODC enzymatic activity and increased cellular levels of putrescine. DFMO and putrescine did not alter c-myc mRNA levels directly, nor did they have any effects on anti-IgM-mediated down-regulation of c-myc mRNA. TNF- α , which inhibited anti-IgM-mediated apoptosis, did not inhibit either anti-IgM or DFMO-mediated inhibition of growth. These agents were without effect on ODC activity itself or on the anti-IgM-mediated increase in ODC activity. From these studies we conclude that ODC inhibition affects growth but is unrelated to the induction of apoptosis. Both anti-IgM-mediated inhibition of growth and induction of apoptosis are independent of ODC. Thus two distinct pathways for growth regulation are present: one in which ODC and polyamines are important and the other cell surface receptor-mediated (sig) which is independent of ODC and polyamines.

L9 ANSWER 27 OF 41 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 96291082 EMBASE
DOCUMENT NUMBER: 1996291082
TITLE: Apparent **inhibition of apoptosis** by
polyamines and aminothiols in DNA fragmentation
assays is artifactual.
AUTHOR: Snyder R.D.; Vogelpohl S.J.; Baldwin B.L.; Deaton E.D.;
Baden E.; Carter J.H.
CORPORATE SOURCE: Abbott Laboratories, Dept 468, 100 Abbott Park Rd, Abbott
Park, IL 60064, United States
SOURCE: Cell Death and Differentiation, (1996) 3/3 (323-330).
ISSN: 1350-9047 CODEN: CDDIEK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We report that, in commonly used DNA fragmentation assays, polyamines and the radioprotective aminothiol WR1065 artifactually depress the degree of spontaneous or induced cellular apoptosis in two distinct ways. Firstly, in assays utilizing Hoechst 33258 dye to measure apoptotic DNA, both amines quench the fluorescence of low affinity dye/DNA binding resulting in preferential underestimation of DNA in the apoptotic DNA fraction and a resultant underestimation of the extent of DNA fragmentation. Secondly, these amines can cause aggregation and condensation of apoptotic DNA, causing anomalous sedimentation under conditions universally employed to separate apoptotic from intact DNA in cell lysates. This anomalous sedimentation of apoptotic DNA leads to underestimation of fragmentation in fluorescence assays as well as in agarose gel assays. We demonstrate that manipulation of the ionic strength of the lysis buffer or lowering the dye concentration ameliorates the effects of dye quenching in the Hoechst assay. Alternatively, this effect is alleviated by substituting DAPI for Hoechst in this assay. Inclusion of a polyanion to the lysis buffer antagonizes the condensation and anomalous sedimentation of apoptotic DNA observed regardless of which dye is used in the assay. These studies call into question the validity of previously reported studies suggesting that polyamines and the radioprotective aminothiol, WR1065, inherently suppress the apoptotic process and, underline the need to consider alternative endpoints of apoptosis such as morphology in order to assess effects on cellular apoptosis of exogenously added agents, particularly di- or polycations.

L9 ANSWER 28 OF 41 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 91285401 EMBASE
DOCUMENT NUMBER: 1991285401
TITLE: Spermine prevents endonuclease activation and apoptosis in
thymocytes.
AUTHOR: Brune B.; Hartzell P.; Nicotera P.; Orrenius S.

CORPORATE SOURCE: Dept. of Toxicology, Box 60 400, S 104 01 Stockholm, Sweden
SOURCE: Experimental Cell Research, (1991) 195/2 (323-329).
ISSN: 0014-4827 CODEN: ECREAL
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Glucocorticoid hormones, Ca²⁺ ionophores, and some toxic chemicals activate a suicide process in thymocytes, known as apoptosis or programmed cell death. A crucial event in apoptosis is the activation of a Ca²⁺- and Mg²⁺-dependent endonuclease that promotes extensive DNA fragmentation. In this study, we investigated the effect of various polyamines on endonuclease activation leading to thymocyte apoptosis. We found that both glucocorticoid- and Ca²⁺ ionophore-induced DNA fragmentation and **apoptosis** were **prevented** by spermine. Other **polyamines** such as putrescine or spermidine had moderate or no effect. Moreover, spermine, and to a lesser extent spermidine, but not putrescine, prevented endonuclease activation in permeabilized liver nuclei incubated in the presence of Ca²⁺ and Mg²⁺, indicating that spermine efficiency in blocking DNA fragmentation was related to the interaction of this polyamine with the endonuclease or its substrate, DNA. Experiments with the fluorescent dye, ethidium bromide, and a purified preparation of liver endonuclease revealed that the protective effect of spermine on DNA fragmentation was related to its ability to modify the chromatin arrangement. Thymocytes incubated with methyl glyoxal bis(guanylhydrazone) to deplete intracellular spermine exhibited spontaneous DNA fragmentation, which suggests that modulation of the intracellular polyamine content and regulation of chromatin structure may play a critical role in the early phases of apoptosis. Finally, these results demonstrate that inhibition of DNA fragmentation also prevents the onset of apoptosis, directly linking endonuclease activation and cell death.

L9 ANSWER 29 OF 41 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 135:298463 CA
TITLE: Polyamine synthesis inhibitor, methylglyoxal bis (cyclopentylamidino hydrazone) (MGBCP) induces apoptosis in cultured rheumatoid synoviocytes and rheumatoid synovial tissue grafted into mice
AUTHOR(S): Tsumuki, H.; Hibasami, H.; Satoh, N.; Sudo, A.; Nakashima, K.; Uchida, A.
CORPORATE SOURCE: Department of Orthopedic Surgery, Faculty of Medicine, Mie University, Tsu-city, 514-0001, Japan
SOURCE: Biogenic Amines (2001), 16(3), 269-284
CODEN: BIAME7; ISSN: 0168-8561
PUBLISHER: VSP BV
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Aim of this study was to investigate effects of a polyamine synthesis inhibitor, methyl-glyoxal bis (cyclopentylamidinohydrazone) (MGBCP), on the growth and induction of programmed cell death (apoptosis) of both cultured rheumatoid synoviocytes in vitro and the rheumatoid synovial tissue grafted into SCID mice in vivo. MGBCP inhibited the growth of RA synoviocytes in a dose-dependent manner by depletion of polyamine contents in the cells. Treatment of RA synoviocytes with MGBCP induced apoptosis in the cultured synoviocytes. Administration of MGBCP at two doses of 20 or 50 mg/kg into the grafted RA tissue induced apoptosis as demonstrated by morphol. change and DNA fragmentation in the tissue. The present data suggest that artificial induction of apoptosis through the injection of MGBCP may remove rheumatoid synovitis. These findings suggest that the inhibition of polyamine synthesis results in the suppression of the growth of RA synoviocytes by inducing apoptosis in the human rheumatoid synovial

tissue in vitro and in vivo.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 30 OF 41 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 135:220904 CA

TITLE: Geraniol, a component of plant essential oils, inhibits growth and polyamine biosynthesis in human colon cancer cells

AUTHOR(S): Carnesecchi, S.; Schneider, Y.; Ceraline, J.; Duranton, B.; Gosse, F.; Seiler, N.; Raul, F.

CORPORATE SOURCE: Laboratory of Nutritional Chemoprevention in Digestive Oncology, Institut de Recherche contre les Cancers de l'Appareil Digestif (IRCAD), Strasbourg, Fr.

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2001), 298(1), 197-200

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Geraniol and other monoterpenes found in essential oils of fruits and herbs have been suggested to represent a new class of agents for cancer chemoprevention. As a first step in clarifying the mode of action of geraniol on colon carcinogenesis, we studied its effects on the growth of a human colon cancer cell line (Caco-2). Geraniol (400 μ M) caused a 70% inhibition of cell growth, with cells accumulating in the S transition phase of the cell cycle, and concomitant inhibition of DNA synthesis. No signs of cytotoxicity or apoptosis were detected. Geraniol caused a 50% decrease of ornithine decarboxylase activity, a key enzyme of polyamine biosynthesis, which is enhanced in cancer growth. This led to a 40% reduction of the intracellular pool of putrescine. Geraniol also activated the intracellular catabolism of polyamines, indicated by enhanced polyamine acetylation. These observations indicate that polyamine metabolism is presumably a target in the antiproliferative properties of geraniol.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 31 OF 41 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 135:86673 CA

TITLE: Effects of α -difluoromethylornithine on the Fas expression and apoptosis in Hep-2 cells

AUTHOR(S): Alvarez, M. G.; Marty, C.; Mori, G.; Rivarola, V.

CORPORATE SOURCE: Facultad de Ciencias Exactas, Fisico-Quimicas y Naturales, Universidad Nacional de Rio Cuarto, Cordoba, Argentina.

SOURCE: Biocell (2000), 24(3), 213-216

CODEN: BOCEEZ; ISSN: 0327-9545

PUBLISHER: Centro Regional de Investigaciones Cientificas y Tecnologicas

DOCUMENT TYPE: Journal

LANGUAGE: English

AB DFMO is an irreversible inhibitor of ornithine decarboxylase (ODC), the key enzyme in mammalian polyamine biosynthesis, and has been shown to induce apoptosis. In this paper, the relation between the effects of DFMO on the polyamine content, apoptotic index and Fas expression in HEP-2 cells was determined. Fas is a type I membrane protein with a mol. mass of 45 kDa, which mediates apoptosis. The results suggest that the treatment with the polyamine inhibitor DFMO induced the expression of the surface antigen Fas, which could be responsible for trigger apoptosis in these cells.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 32 OF 41 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 134:40092 CA

TITLE: Inhibition of ornithine decarboxylase by α -difluoromethylornithine induces apoptosis of HC11 mouse mammary epithelial cells

AUTHOR(S): Ploszaj, T.; Motyl, T.; Zimowska, W.; Skierski, J.; Zwierzchowski, L.

CORPORATE SOURCE: Department of Animal Physiology, Faculty of Veterinary Medicine, Warsaw Agricultural University, Warsaw, Pol.

SOURCE: Amino Acids (2000), 19(2), 483-496

CODEN: AACIE6; ISSN: 0939-4451

PUBLISHER: Springer-Verlag Wien

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of α -difluoromethylornithine (DFMO) on the apoptosis of HC11 mouse mammary epithelial cells was investigated. The involvement of reactive oxygen species (ROS) and Bcl-2 protein in the mechanism of apoptosis induced by ornithine decarboxylase (ODC) inhibition was also assessed. DFMO (0.1, 1 and 5 mM) induced apoptosis of HC11 cells in dose- and time-dependent manner. Apoptosis manifests itself with morphol. features like: cell shrinkage, condensation of chromatin, pyknosis and fragmentation of nucleus, followed by secondary necrosis (putrosis). The decrease in the nuclear DNA contents appearing as the hypo-diploidal peak sub-G1 in the DNA histogram was not dependent on the presence of prolactin (5 μ g/mL) in DFMO-treated cultures. Apoptosis induced by ODC inhibition was associated with a rapid increase in ROS concentration in HC11 cells observed within

1 h after DFMO treatment. The down-regulation of Bcl-2 as a decrease in cell number expressing bcl-2 and a lowered Bcl-2 protein content in cells expressing this protooncogene was also noted. The administration of putrescine (50 μ M) lowered the number of early-apoptotic, late-apoptotic and necrotic cells. Moreover, it increased the number of cells expressing bcl-2. In conclusion, the disturbance of cellular polyamine homeostasis by inhibition of their synthesis enhances mammary epithelial cell susceptibility to apoptosis. It may occur in the mammary gland at the end of lactation, when the depletion of circulating lactogenic hormones and activation of intra-mammary apoptogenic factors expression take place.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 33 OF 41 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 133:202702 CA

TITLE: Cytotoxicity of novel unsymmetrically substituted inhibitors of polyamine biosynthesis in human cancer cells. [Erratum to document cited in CA132:189382]

AUTHOR(S): Nairn, Lynsey M.; Lindsay, Gayle S.; Woster, P. M.; Wallace, Heather M.

CORPORATE SOURCE: Department of Medicine and Therapeutics, University of Aberdeen, Aberdeen, AB25 2ZD, UK

SOURCE: Journal of Cellular Physiology (2000), 183(1), 143

CODEN: JCLLAX; ISSN: 0021-9541

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In Fig. 3 on page 212, the four sep. parts of the figure should have been referred to individually; the corrected figure and legend are given.

L9 ANSWER 34 OF 41 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 133:116086 CA

TITLE: The effects of polyamine synthesis inhibitors on the rat jejunum: histological effects of inhibitors of polyamine biosynthesis on normal and hyperplastic rat jejunum

AUTHOR(S): Ewen, S. W. B.; Grant, G.; Pusztai, A.; Bardocz, S.
 CORPORATE SOURCE: Department of Pathology/Medicine and Therapeutics,
 Medical School, University of Aberdeen, Aberdeen, AB25
 2ZD, UK
 SOURCE: Polyamines in Health and Nutrition (1999),
 99-104. Editor(s): Bardocz, Susan; White, Ann.
 Kluwer Academic Publishers: Hingham, Mass.
 CODEN: 68WQAI
 DOCUMENT TYPE: Conference
 LANGUAGE: English
 AB Rats given injections of difluoromethylornithine (DFMO), MGBG and CGP
 48664A showed decreases in jejunal crypt length, in order of decreasing
 effectiveness. DFMO also increased the number of apoptoses per 50 crypts.
 REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 35 OF 41 CA COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 132:342903 CA
 TITLE: α -Difluoromethylornithine induces apoptosis as
 well as antiangiogenesis in the inhibition of tumor
 growth and metastasis in a human gastric cancer model
 AUTHOR(S): Takahashi, Yutaka; Mai, Masayoshi; Nishioka, Kenji
 CORPORATE SOURCE: Department of Surgical Oncology, Cancer Research
 Institute, Kanazawa University, Kanazawa, 921-8044,
 Japan
 SOURCE: International Journal of Cancer (2000),
 85(2), 243-247
 CODEN: IJCNAW; ISSN: 0020-7136
 PUBLISHER: Wiley-Liss, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB α -Difluoromethylornithine (DFMO), an inhibitor of polyamine
 biosynthesis, inhibited the growth of human umbilical vein endothelial
 cells and angioendothelial cells in vitro and of KKLS, a gastric cancer
 cell line, in culture, and also the growth of KKLS cells transplanted into
 nude mice. DFMO also inhibited liver metastasis of KKLS orthotransplanted
 in the stomach of nude mice. The vessel d. of DFMO-treated tumors was
 lower than that of nontreated tumors. The apoptotic index was greater in
 DFMO-treated tumors than in nontreated tumors. These results suggest that
 antiangiogenesis and apoptosis play significant roles in the inhibition by
 DFMO of the growth and metastasis of this human gastric cancer model and
 provide evidence that DFMO induces apoptosis.
 REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 36 OF 41 CA COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 132:189382 CA
 TITLE: Cytotoxicity of novel unsymmetrically substituted
 inhibitors of polyamine biosynthesis in human cancer
 cells
 AUTHOR(S): Nairn, Lynsey M.; Lindsay, Gayle S.; Woster, P. M.;
 Wallace, Heather M.
 CORPORATE SOURCE: Department of Medicine and Therapeutics, University of
 Aberdeen, Aberdeen, AB25 2ZD, UK
 SOURCE: Journal of Cellular Physiology (2000),
 182(2), 209-213
 CODEN: JCLLAX; ISSN: 0021-9541
 PUBLISHER: Wiley-Liss, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The cytotoxicity of two novel polyamine analogs was compared with that of
 a known cytotoxic drug, etoposide, in a human promyelogenous leukemic cell
 line. CHEN-spm showed significant acute cytotoxicity in these cells and
 was comparable to etoposide in terms of IC50 value. The cell death observed

from both CHEN-spm and etoposide was typically apoptotic with increased DNA fragmentation, altered cell morphol., and cell cycle distribution. CPEN-spm, on the other hand, exhibited no toxic effects over the short-term (24 h) exposure period. Intracellular polyamine content decreased in the presence of all inhibitors but only CPEN-spm produced significant induction of spermidine/spermine N1-acetyltransferase in 24 h. Thus, increased polyamine catabolism appears not to be essential for the initiation of apoptotic cell death in these human leukemic cells.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 37 OF 41 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 131:179457 CA

TITLE: Effects of polyamines, polyamine synthesis inhibitors, and polyamine analogs on casein kinase II using myc oncoprotein as substrate

AUTHOR(S): Gundogus-Ozcanli, Nesrin; Sayilir, Cafer; Criss, Wayne E.

CORPORATE SOURCE: Department of Medical Biology, Istanbul University Medical School, Istanbul, Turk.

SOURCE: Biochemical Pharmacology (1999), 58(2), 251-254

CODEN: BCPA6; ISSN: 0006-2952

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Polyamines, casein kinase II (CKII), and the myc oncogene are directly involved in the regulation of mol. events in cell proliferation, differentiation, and apoptosis. Each is increased in rapidly growing cancer cells. In our current study, we showed that the Km values for purified CKII were similar for casein and Myc oncoprotein under a variety of assay conditions, and that specific natural and synthetic polyamines stimulated CKII phosphorylation of Myc oncoprotein 2- to 20-fold via increases in Vmax. When polyamine synthesis inhibitors and analogs were studied with this purified enzyme system, two polyamine analogs (N1,N12-bis-(ethyl)-spermine [BESpm] and 1,19-bis-(ethylamino)-5,10,15, triazononadecane [BE4X4]), which did not affect basal enzyme activity, did prevent (or inhibit) polyamine-stimulated CKII activity by approx. 70 and 85 percent, resp. Because the Myc oncoprotein trans activates several genes for key proteins involved in the regulation of cellular proliferation, including the ornithine decarboxylase gene (rate-limiting enzyme of polyamine synthesis), we suggest that there may be linkages between polyamines, CKII, and Myc in the control of cellular proliferation. We also suggest that the anticancer drugs BESpm and BE4X4 may inhibit cancer cell proliferation partially through interference with the above-suggested CKII linkages.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 38 OF 41 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 131:56965 CA

TITLE: Inhibition of polyamine synthesis induces p53 gene expression but not apoptosis

AUTHOR(S): Li, Li; Li, Ji; Rao, Jaladanki N.; Li, Minglin; Bass, Barbara L.; Wang, Jian-Ying

CORPORATE SOURCE: Department of Surgery, University of Maryland School of Medicine and Baltimore Veterans Affairs Medical Center, Baltimore, MD, 21201, USA

SOURCE: American Journal of Physiology (1999), 276(4, Pt. 1), C946-C954

CODEN: AJPHAP; ISSN: 0002-9513

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The nuclear phosphoprotein p53 acts as a transcription factor and is involved in growth inhibition and apoptosis. The present study was designed to examine the effect of decreasing cellular polyamines on p53 gene expression and apoptosis in small intestinal epithelial (IEC-6) cells. Cells were grown in DMEM containing 5% dialyzed fetal bovine serum in the presence or absence of α -difluoromethylornithine (DFMO), a specific inhibitor of polyamine biosynthesis, for 4, 6, and 12 days. The cellular polyamines putrescine, spermidine, and spermine in DFMO-treated cells decreased dramatically at 4 days and remained depleted thereafter. Polyamine depletion by DFMO was accompanied by a significant increase in expression of the p53 gene. The p53 mRNA levels increased 4 days after exposure to DFMO, and the maximum increases occurred at 6 and 12 days after exposure. Increased levels of p53 mRNA in DFMO-treated cells were paralleled by increases in p53 protein. Polyamines given together with DFMO completely prevented increased expression of the p53 gene. Increased expression of the p53 gene in DFMO-treated cells was associated with a significant increase in G1 phase growth arrest. In contrast, no features of programmed cell death were identified after polyamine depletion: no internucleosomal DNA fragmentation was observed, and no morphol. features of apoptosis were evident in cells exposed to DFMO for 4, 6, and 12 days. These results indicate that 1) decreasing cellular polyamines increases expression of the p53 gene and 2) activation of p53 gene expression after polyamine depletion does not induce apoptosis in intestinal crypt cells. These findings suggest that increased expression of the p53 gene may play an important role in growth inhibition caused by polyamine depletion.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 39 OF 41 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 130:90158 CA

TITLE: Involvement of apoptosis and cyclin D1 gene repression in growth inhibition of T-47D human breast cancer cells by methylglyoxal bis(cyclopentylamidino)hydrazine

AUTHOR(S): Kaneko, Hiroshi; Hibasami, Hiroshige; Satoh, Norifumi; Wakabayashi, Hiroshi; Ikeda, Hiroko; Tsuge, Naoko; Yonemaru, Kaori; Muraki, Akemi; Kawarada, Yoshifumi; Nakashima, Kunio

CORPORATE SOURCE: Departments of Biochemistry, Faculty of Medicine, Mie University, Mie, 514-8507, Japan

SOURCE: International Journal of Molecular Medicine (1998), 1(6), 931-936

CODEN: IJMMFG; ISSN: 1107-3756

PUBLISHER: International Journal of Molecular Medicine

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Polyamines are considered to be important intracellular mols. for the proliferation of the cancer cells. In this study, effects of methylglyoxal bis(cyclopentylamidino)hydrazine (MGBCP), a potent inhibitor of the polyamine biosynthetic pathway, on the growth and cell cycle of T-47D human breast cancer cells were investigated. MGBCP dose-dependently inhibited the growth of T-47D cells, in which the contents of spermine, spermidine and putrescine decreased concomitantly. The gene expression of cyclin D1 was also repressed by the MGBCP treatment. The MGBCP-treated cells clearly exhibited morphol. changes indicating the blebbing and chromatin condensation which are characteristic of apoptosis. Flow cytometric anal. showed hypo-diploid subpopulations due to apoptotic cells, and characteristic oligonucleosomal-sized DNA fragments were clearly observed for MGBCP-treated cells as the concentration of the drug was increased. These findings suggest that the inhibition of polyamine synthesis results in the repressions of cyclin D1 expression and cell cycle progression, eventually inducing apoptosis in these human breast cancer cells.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 40 OF 41 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 127:199705 CA

TITLE: Induction of apoptotic cell death in three human osteosarcoma cell lines by a polyamine synthesis inhibitor, methylglyoxal bis(cyclopentylamidinohydrazo ne) (MGBCP)

AUTHOR(S): Mori, Kentaro; Hibasami, Hiroshige; Satoh, Norifumi; Sonoda, Jun; Yamasaki, Takashi; Tajima, Masatoshi; Higuchi, Shigeomi; Wakabayashi, Hiroki; Kaneko, Hiroshi; Uchida, Atsumasa; Nakashima, Kunio

CORPORATE SOURCE: Department of Orthopedic Surgery, Faculty of Medicine, Mie University, Tsu, 514, Japan

SOURCE: Anticancer Research (1997), 17(4A), 2385-2390

CODEN: ANTRD4; ISSN: 0250-7005

PUBLISHER: Anticancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Our previous expts. have shown that methylglyoxal bis(cyclopentylamidinohydrazone) (MGBCP), a polyamine synthesis inhibitor, suppresses the growth of osteosarcoma cells repressing their intracellular polyamine levels, and that this inhibition of cell growth is only partially reversed by the addition of polyamines. In the present study, we found evidence indicating that the incomplete recovery of cell growth by the addition of polyamines to the polyamine-depleted cells was due to programmed cell death (apoptosis) induced by MGBCP. Morphol. changes showing blebbing and chromatin condensation were observed in MGBCP-treated cells, and hypodiploid subpopulations containing apoptotic cells were clearly visible in the profile of flow cytometric anal. Characteristic oligonucleosomal-sized fragments were increased as the concentration of MGBCP was increased. The results presented here suggest that in addition to reducing the growth rates, MGBCP can induce apoptotic cell death in three human osteosarcoma cell lines.

L9 ANSWER 41 OF 41 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 125:82861 CA

TITLE: Polyamine acetylation and apoptosis

AUTHOR(S): Lindsay, Gayle S.; Wallace, Heather M.

CORPORATE SOURCE: Dep. of Medicine and Therapeutics, Aberdeen Univ. Medical Sch., Foresterhill/Aberdeen, AB9 2ZD, UK

SOURCE: Biochemical Society Transactions (1996), 24(2), 229S

CODEN: BCSTB5; ISSN: 0300-5127

PUBLISHER: Portland Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The anticancer drug etoposide was used to induce apoptosis in the human promyelogenous leukemic HL60 cell line. The observed late induction of spermidine/spermine N1-acetyltransferase (SAT) suggest that SAT is more likely to be a necrotic response rather than an early signal for the initiation of apoptosis. No change in polyamine levels or RNA formation were observed. A decline in both protein and DNA formation was observed

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